Survival among Black and White Patients with Renal Cell Carcinoma in an Equal-Access Health Care System

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ABSTRACT

Purpose: Unequal access to health care may be a reason for shorter survival among black patients with renal cell carcinoma (RCC) than among their white counterparts. No studies have investigated survival disparity among RCC patients in an equal-access health care delivery system. This study aimed to examine racial differences in survival among clear cell RCC patients in the Department of Defense's (DoD) Military Health System (MHS), which provides equal access to care to all persons.

Methods: The study used the DoD's Automated Central Tumor Registry to identify 2,056 white patients and 370 black patients diagnosed with clear cell RCC between 1988 and 2004. the. Subjects were followed through 2007 with a median follow up time of 4.8 years. Kaplan-Meier survival curves were compared and a Cox model was used to estimate the hazard ratios (HRs) associated with survival by race.

Results: During follow up, 1,027 white and 158 black patients died. The Kaplan-Meier curves showed that black patients had more favorable overall survival than did whites (Log Rank P=0.034). After adjustment for demographic, tumor, and treatment variables, the Cox model showed no statistically significant racial difference overall (adjusted HR=1.08, 95% CI=0.90 to 1.29) or stratified by age, sex or tumor stage. However, among patients who did not undergo surgery, black patients had poorer survival than whites.

Conclusions: The lack of racial difference in survival among RCC patients in the MHS may be related to equal access to health care. Improved access could reduce the survival disparity among RCC patients in the general population.

Introduction

In 2015, approximately 61,560 cancers of the kidney and renal pelvis will be diagnosed in the United States, and 14,080 deaths due to these cancers will occur [1]. Nearly ninety percent of these tumors are renal cell carcinomas (RCC)[2] . RCC is the third leading cause of death among genitourinary malignancies and is the most lethal urologic malignancy [3,4]. Research has shown that black patients with RCC tend to have a poorer prognosis and a shorter overall survival than their white counterparts [5,6,7,8]. A recent Surveillance, Epidemiology, and End Results (SEER) analysis reported that blacks with RCC consistently had higher all-cause mortality rates than whites in the general population[5]. Similar overall survival disparity among RCC patients was observed in several other studies based on earlier SEER data [7,8] and state-wide cancer registry data [6]. The reasons for this disparity in mortality are unknown but may be related to racial differences in access to health care and treatment [5,6,7,8,9,10], differences in quality of care received [5,7], patients' attitudes toward and beliefs in treatment decisions [5,7], comorbid conditions [5,7,8,11], and stressful life events associated with socioeconomic status[5,6,7].

Among factors that may be associated with racial disparity in cancer outcomes, unequal access to health care may be a major one [5,6,7,8,9]. Inadequate access to health care by racial minorities may result in delayed diagnosis, advanced tumor stage, suboptimal treatment [12] and may result in poor survival. In the general population, black persons are more likely than white persons to have inadequate insurance coverage and are more likely to receive lower quality of care [13,14]. Thus, black persons are less likely to receive timely and optimal cancer treatments [13,14], which may result in a higher risk of having unfavorable disease outcomes. In an equal access system, different racial groups have the similar level of access to medical care, presumably with the similar quality of care. Identification of whether there are racial differences in outcome in an equal access system is important for evaluating the role of equal

access to care in the racial disparities. Previous research has shown that with equal access to care and treatment, blacks and whites have similar survival experiences for lung cancer[15,16,17], colon cancer[18,19], and prostate cancer[20]. To date, there has been no research in an equal-access system to investigate survival among patients with RCC.

The Department of Defense's (DoD) Military Health System (MHS) provides equal health care access to military service members, retirees, and their dependents. Therefore, MHS offers an excellent resource for examining whether racial disparity in RCC survival exists. In addition to assessing whether there were differences in survival, we also evaluated whether the racial groups differed in survival by demographic variables, tumor characteristics, and treatments.

Materials and Methods

Sources of data

The sources of data have been described previously [16]. Briefly, data on patients diagnosed with RCC between 1988 and 2004 were obtained from the DoD's Automated Central Tumor Registry (ACTUR), a database and clinical tracking system for all cancer patients who are diagnosed and/or received cancer treatment at military treatment facilities, including active-duty members, retirees and their dependents. The ACTUR data are reviewed by specialized registrars to verify diagnosis. Patients are followed by ACTUR until death. Dates of diagnosis, last contact, and death are recorded. Death information is obtained from a variety of sources including, but not limited to reporting hospitals and physicians, department of motor vehicles, Medicare/Medicaid file, and death certificates. The current study included the following variables from ACTUR: age at diagnosis, sex, race, ethnicity, marital status, active duty status, military service branch, tumor stage (localized, regional and distant, unknown), grade (well differentiated, moderately differentiated, poorly differentiated, undifferentiated, differentiation unknown) and tumor size (in unit of millimeter), receipt of surgery, types of surgery, receipt of chemotherapy, receipt of radiation therapy, and tumor recurrence. The study was approved the

4

by the institutional review boards of U.S. Military Cancer Institute, Walter Reed National Military Medical Center, the Armed Forces Institute of Pathology and the National Institutes of Health Office of Human Subjects Research.

Study Subjects

Eligible study subjects were black and white patients who are diagnosed with histologically confirmed primary clear cell RCC between January 1, 1988 and December 31, 2004. Clear cell RCC constitutes over 85% of all RCC [5,21]. We confined analysis to clear cell RCC because of the relatively small numbers of patients with other histologic types and considerations in minimizing potential confounding by histology [21,22]. Cancer site and histology were classified using the topography (C64.9) and morphology codes (8310-8312) of the International Classification of Diseases for Oncology, third edition (ICD-O-3)[23]. Patients with a history of another primary cancer(s) were excluded to minimize the potential effect on survival of other cancers. A total of 2,426 patients were included in the final analysis. Data through December 31, 2007 were included in the analysis..

Statistical Analysis

The study outcome was all-cause mortality. The observed survival time was calculated as the difference between date of diagnosis and date of death for persons who died during the study period. For persons who did not die during the study period, survival time was censored at the date of last contact or the end of the study, December 31, 2007. The distributions of demographic variables, tumor characteristics, and treatment variables by race were compared and tested using the Chi-square test. Age-standardized p-values were also provided using all study subjects as the standard population. Kaplan-Meier survival curves were constructed and compared between blacks and whites and the log-rank test was used to test significant difference between survival curves. A Cox proportional hazards model was used to estimate

mortality risk associated with race. We calculated the hazard ratios (HRs) and their 95% confidence intervals (95% CI) in a univariate model and multivariate models. In multivariate models, we obtained the HRs and 95% CIs by adjusting for age only, demographic variables only (age, gender, ethnicity, active duty status, marital status) and all demographic, tumor and treatment variables (age, gender, ethnicity, active duty status, marital status tumor stage, grade, size, recurrence, and receipt of surgery/chemotherapy/radiation therapy). In all models, age was adjusted as a continuous variable and all other variables were categorical. Cox regression analysis was further performed with stratification by age, sex, Hispanic origin, tumor stage, and receipt of surgery. Statistical analyses were conducted using SAS software version 9.3.0 (SAS Institute, Inc.). All reported P values are two sided, with the significance level set at P<0.05.

Results

The study participants consisted of 2,056 white patients and 370 black patients (Table 1). Compared to whites, blacks tended to be younger with 31.9% of blacks diagnosed before age 50 years compared to 21.4% of whites (p<0.0001)(Table 1). Blacks were more likely to be non-Hispanic, (p<0.0001), divorced or separated (p=0.003) and be in the Army (p=0.0003). Although not statistically significant, blacks were more likely be diagnosed at localized stages (64.9% vs. 58.2%), and to have smaller tumors (≤30mm) (p=0.0083), but there was no significant difference in tumor grade distribution (p=0.1888). There were no significant racial differences in sex, active duty status, the receipt of surgery, the receipt of chemotherapy, the receipt of radiation therapy, or recurrence. The results remained similar when age was standardized (Table 1).

During the follow-up period, 1,030 whites and 158 blacks died. The Kaplan-Meier curve (Figure 1) showed significantly better overall survival among blacks than whites (log rank P=0.031). Table 2 shows the results from Cox regression analyses. In univariate model, blacks had significantly better survival than whites, with a HR of 0.83 (95% CI=0.71 to 0.98). The HR

was attenuated with the 95% confidence interval containing the unity after adjusting for age (HR=0.93, 95% CI=0.79 to 1.10). The HR was 0.97 (95% CI= 0.82 to 1.16) with additional adjustment for sex, Hispanic origin, marital status and active duty status. Further adjusting for tumor characteristics and treatment variables resulted in a HR of 1.07 (95% CI=0.90 to 1.28) for blacks relative to whites. In general, there were no racial differences when the full multivariate model was further stratified by age, sex or tumor stage (Table 3). However, in patients not receiving surgery, blacks exhibited a 1.56-fold (95% CI=1.09 to 2.24) greater risk of death than whites.

Discussion

In this study, we found no statistically significant racial differences in survival among patients with clear cell RCC after adjustment for demographic, tumor and treatment factors. This finding was generally observed across subgroups defined by age, sex or tumor stage.

In prior studies, blacks have been consistently reported to have poorer overall survival than whites in large population-based studies [5,6,7,8,10]. In a study of using the SEER-Medicare database, 964 black and 10,482 white RCC patients aged 65 and older were identified After adjustment for demographic variables and cancer prognostic factors, overall survival was poorer among blacks than whites [7]. Poorer relative survival among blacks was also observed in a study using data from the California Cancer Registry data of 39,432 patients with RCC diagnosed between 1988 to 2004 [6].   In addition, a SEER-based study of RCC [8] reported poorer overall survival among Black patients than their White counterparts. While this racial disparity may be related to multiple factors such as quality of care [5,7], health care behavior and beliefs [5,7], comorbidity [5,7,8,11], social environment [5,7] and biological predisposition [6,24], accessibility to health care [5,6,7,8,9,10] may be most influential. Poorer access to health care by racial minorities has been frequently associated with delayed diagnosis,

advanced disease stage, suboptimal treatment, and poor prognosis [12,25,26] [27]. A recent study based on SEER data of nearly 40,000 RCC patients [5] diagnosed from 1992 to 2007 found that blacks consistently had higher all-cause mortality than whites even though both groups had the same tumor stage, tumor size, or surgical treatment. It should be noted, however that the study only conducted univariate analyses with stratification on a single factor such as tumor stage.   In addition, even among persons with tumors of the same stage who receive surgery, race may be a determinant of timing, interval, frequency and quality of various treatment including surgery, follow-up and surveillance.

While equal access does not necessarily mean equal utilization of medical care, smaller or no difference in survival between racial groups in an equal access system would suggest equal access may reduce racial disparities. Indeed, persons with common cancers have been observed to have similar survival experiences in studies conducted in equal access systems [15,16,17,18,19,20]. To the best of our knowledge, our study is the first one among RCC patients in such a system. Our study found no overall racial difference in survival after adjustment for demographic, tumor and treatment factors. The results suggest that the survival disadvantage among blacks in the general population may be associated with poorer access to care.

Although no overall racial differences were observed in our study, we did find that blacks who did not receive surgery experienced worse survival than their white counterparts. While the hazard ratios between subgroups by surgery were not significantly different, some racial disparity may exist. Patients who do not receive surgery are more likely to have renal failure at diagnosis due to the severity of the underlying kidney disease [28,29]. It is possible that the survival difference observed in this stratum may reflect a larger proportion of black persons with renal failure at diagnosis. In contrast to our study, however, a study in a Medicare population [7] found that blacks who did not receive surgery had better crude survival than did whites, but the

difference in survival was reduced substantially after adjustment for cancer stage, tumor size and demographic variables. Nevertheless, in a recent SEER study[5] without adjustment for tumor stage and other factors, among persons who received surgery , blacks had poorer survival than whites. While the reasons for the differences in results between this study and our study are not clear, we do not exclude the possibility that the racial disparity in all-cause death might result from differences in factors not included in the current study, such as comorbid conditions or timing and frequency of treatment of renal cancer.

Compared to whites, blacks in the current study were diagnosed at earlier stages and with smaller tumors, characteristics that are frequently linked to better prognosis. Earlier stage at diagnosis among blacks compared to whites has also been consistently observed in previous studies of the general population [5,6,7,8,10,30]. Better survival among blacks in our study might result from diagnosis at earlier tumor stages because the survival advantage of blacks was no longer observed after adjustment for tumor stage and other variables. However, in previous studies in the general population, the poorer survival of blacks persisted despite their earlier tumor stage [5,6,7,8,30]. Perhaps in the general population, the survival benefit of early stage is not sufficient to counterbalance the disadvantage of other unfavorable factors, including limited access to health care.

This study has several strengths. First, the study was performed in an equal-access health care system, thus the impact of unequal access on survival disparity is largely minimized or controlled, which is unlikely to exist in studies of general population. Second, as a registry based study, the availability of demographic, tumor and treatment data from DoD's cancer registry allows for control for confounding and permits stratified analysis to identify racial disparity in subgroups. It should be noted, however, that we had limited statistical power in certain subgroup analyses due to relatively small numbers. Also, data were not available to address the role of other potential factors (such as comorbid conditions, social economic status,

life styles, and health care behaviors, etc.) on survival disparity in RCC patients and renal cancer specific death cannot be evaluated.

To the best of our knowledge, this is the first study of survival among RCC patients in an equal access system. We found no racial differences in overall survival among black and white patients with clear cell RCC. Our results suggest that unequal access to health care plays an important role in survival disparity and that better access to health care could reduce this disparity in the general population.

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Figure Legend

Fig1. Kaplan-Meier survival curves comparing black and white clear cell RCC patients diagnosed from 1988 to 2004 in the U.S. Department of Defense Cancer Registry